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A1
applications are incorporated herein by reference.

In the Claims

Cancel Claims 24-34. Add Claims 35-53.

- A2
35. A stable pharmaceutical formulation comprising:
- a) a GLP-1 compound selected from the group consisting of: GLP-1, GLP-1 analogs, and GLP-1 derivatives wherein the GLP-1 compound can bind to the GLP-1 receptor;
 - b) a tween polymeric surfactant;
 - c) a preservative; and
 - d) a buffer
- wherein the stable formulation is a solution and has a pH between about 6.5 and about 9.0.
36. The formulation of Claim 35, wherein the GLP-1 compound is protected from the activity of dipeptidyl-peptidase IV.
37. The formulation of Claim 35, wherein the GLP-1 compound comprises the sequence of SEQ ID NO:1 or SEQ ID NO:4.
38. The formulation of Claim 36 wherein the GLP-1 compound comprises the sequence of SEQ ID NO:5.
39. The formulation of Claim 35 wherein the GLP-1 compound is GLP-1(7-34), GLP-1(7-35), GLP-1(7-36), GLP-1(7-37), or the amide forms thereof, with at least one modification selected from the group consisting of:
- SEQ ID NO:1

- A2
- (a) substitution of a glycine, serine, cysteine, threonine, asparagine, glutamine, tyrosine, alanine, valine, isoleucine, leucine, methionine, phenylalanine, arginine, or D-lysine for lysine at position 26 and/or position 34 or substitution of a glycine, serine, cysteine, threonine, asparagine, glutamine, tyrosine, alanine, valine, isoleucine, leucine, methionine, phenylalanine, lysine, or a D-arginine for arginine at position 36;
- (b) substitution of an oxidation-resistant amino acid for tryptophan at position 31;
- (c) substitution according to at least one of:
Y for V at position 16;
K for S at position 18;
D for E at position 21;
S for G at position 22;
R for Q at position 23;
R for A at position 24; and
Q for K at position 26;
- (d) substitution comprising at least one of:
glycine, serine, or cysteine for alanine at position 8;
aspartic acid, glycine, serine, cysteine, threonine, asparagine, glutamine, tyrosine, alanine, valine, isoleucine, leucine, methionine, or phenylalanine for glutamic acid at position 9;
serine, cysteine, threonine, asparagine, glutamine, tyrosine, alanine, valine,

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isoleucine, leucine, methionine, or
phenylalanine for glycine at position 10; and
glutamic acid for aspartic acid at position 15;
and

- (e) substitution ^{of a} glycine, serine, cysteine,
threonine, asparagine, glutamine, tyrosine,
alanine, valine, isoleucine, leucine,
methionine, or phenylalanine or the D or N-
acylated or alkylated form of histidine for
histidine at position 7.

40. The formulation of Claim 39, wherein the GLP-1
analog is acylated at an amino acid side group.
41. The formulation of Claim 40, wherein the GLP-1
analog is acylated on the epsilon-amino group of
lysine.
42. The formulation of Claim 41, wherein the lysine that
is acylated is lysine 34.
43. The formulation of Claim 42, wherein the epsilon-
amino group of lysine is acylated with an acyl group
selected from the group consisting of C₆-C₁₀
unbranched acyl.
44. The formulation of Claim 35 wherein the GLP-1
^{compound} molecule is a GLP-1 derivative prepared by the
process of acylating a GLP-1 analog selected from
the group consisting of GLP-1(7-34), GLP-1(7-35),
GLP-1(7-36), GLP-1(7-37), and the amide forms
thereof, with at least one modification selected
- claim 35

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from the group consisting of:

- (a) substitution of a glycine, serine, cysteine, threonine, asparagine, glutamine, tyrosine, alanine, valine, isoleucine, leucine, methionine, phenylalanine, arginine, or D-lysine for lysine at position 26 and/or position 34 or substitution of a glycine, serine, cysteine, threonine, asparagine, glutamine, tyrosine, alanine, valine, isoleucine, leucine, methionine, phenylalanine, lysine, or a D-arginine for arginine at position 36;
- (b) substitution of an oxidation-resistant amino acid for tryptophan at position 31;
- (c) substitution according to at least one of:
Y for V at position 16;
K for S at position 18;
D for E at position 21;
S for G at position 22;
R for Q at position 23;
R for A at position 24; and
Q for K at position 26;
- (d) substitution comprising at least one of:
glycine, serine, or cysteine for alanine at position 8;
aspartic acid, glycine, serine, cysteine, threonine, asparagine, glutamine, tyrosine, alanine, valine, isoleucine, leucine, methionine, or phenylalanine for glutamic acid at position 9;
serine, cysteine, threonine, asparagine, glutamine, tyrosine, alanine, valine,

AD
isoleucine, leucine, methionine, or
phenylalanine for glycine at position 10; and
glutamic acid for aspartic acid at position 15;
and

- (e) substitution ^{of a} glycine, serine, cysteine,
threonine, asparagine, glutamine, tyrosine,
alanine, valine, isoleucine, leucine,
methionine, or phenylalanine or the D or N-
acylated or alkylated form of histidine for
histidine at position 7.

45. The formulation of Claim 44 wherein the GLP-1 analog
has an arginine substituted for lysine at position
34.
46. The formulation of Claim 45 wherein the GLP-1 analog
is acylated on the epsilon-amino group of lysine.
47. The formulation of Claim 35, wherein the GLP-1
compound is a GLP-1 derivative.
48. The formulation of Claim 35 further comprising an
isotonicity agent.
49. The formulation of Claim 48 wherein the isotonicity
agent is glycerin.
50. The formulation of Claim 48 wherein the isotonicity
agent is sodium chloride.
51. The formulation of Claim 35 ~~further~~ wherein the
preservative is phenol.

Ad 52. The formulation of Claim 35 ~~further~~ wherein the preservative is m-cresol.

WD 53. A method of treating a person having a condition for which administration of a GLP-1 compound is indicated, said method comprising administering a pharmacologically effective amount of a formulation of Claim 35.

Claim Amendments

Applicants wish to continue co-pending application, U.S. Serial No. 09/573,809, filed June 1, 2000. Please delete Claims 24-34 and add new Claims 34-53. Support for the new claims is found through-out the specification. In particular support for the formulation comprising tween polymeric surfactants can be found on page 3, line 19, page 6 lines 26 to 27, and page 15 line 14 to page 16 line 6. Support for DPP IV protected GLP-1 compounds can be found on page 11, lines 5 to 11. Support for the genus of GLP-1 compounds can be found on page 9, line 26, to page 11, line 4.

Sequence Listing

Pursuant to 37 C.F.R. §1.821(e), Applicants refer to and rely on a computer readable Sequence Listing provided to the U.S. Patent and Trademark Office in a prior application to which the instant case claims priority, US Serial No. 09/573,809, filed June 1, 2000. The instant application has been amended to insert the corresponding paper readable copy, which is enclosed herewith, into the instant application. The remainder of the requirements of requirements of 37 C.F.R. §1.821 through §1.825 are satisfied by the enclosed "STATEMENT TO SUPPORT FILING AND SUBMISSION IN ACCORDANCE WITH 37 C.F.R. 1.821(f) SEQUENCE LISTING)"

X-11368A

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Favorable consideration of the subject application is requested.

Respectfully submitted,



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